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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/751,346	01/02/2004	Ron S. Israeli	41426-FA-PCT-US/JPW/CY	7618

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EXAMINER	
YAO, LEI	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 11/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/751,346	ISRAELI ET AL.	
	Examiner	Art Unit	
	Lei Yao, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-31* is/are pending in the application.

4a) Of the above claim(s) *26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-25 and 27-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/04, 9/05, 12/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of group I in the reply filed 9/12/05 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicants are also required to elect a single species from group A, a single species from group B, and a single species from C, in the event that applicants elect Group I. However, applicants elect the genus of whole group A and whole group B instead of a single species from Group A and B for examination, which do not meet the requirement of election of species in the office action filed 3/8/05. During a telephone conversation with Brian Amon on Oct 4, 2005, a provisional election was made to prosecute species antibody from group A and toxin from group B. Affirmation of this election must be made by applicant in replying to this Office action.

Claims 1-22 and 32-58 have been cancelled. Claims 21-31 are pending. Claim 26 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species there being no allowable generic or linking claim. Claims 21-25, 27-31 examined on the merits.

Information Disclosure Statement

The information disclosure statement (s) (IDS) submitted on 1/2/04, 6/18/04, 12/10/04, 3/29/04, 9/12/05 are/is considered by the examiner and initialed copy of the PTO-1449 is enclosed.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

The applicants listed in the newly amended specification on page 1 indicating priority of should be in the declaration. A new declaration is required in correlation with the amended specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21, 23-24, 27-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody for a prostate specific membrane antigen (PSM) does not reasonably provide enablement for other **biological agent**. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factor considered when determining if the disclosure satisfies the enablement requirement and whether any is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of necessary experimentation claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re wands,* 858 F.2d 731, 737.8 USPQ2d 1400, 1404 (Fed. Cir.1988).

The claims are broadly drawn to a method of ablating or killing normal, benign hyperlplastic, and cancerous prostate epithelial cells comprising binding **a biological agent** to an outer membrane domain of prostate specific membrane antigen (PSM) in the cells, wherein the biological agent is liked to a cytotoxic agent. The specification teaches that antibodies against PSM coupled with a cytotoxic agent will be useful to eliminate prostate cancer cells (page 68, line 16-24). The specification also teaches a therapeutic agent comprising antibodies or ligand(s) directed against PSM antigen and a cytotoxic agent conjugated thereto or antibodies linked enzymes, which activate prodrug to kill the tumor and the cytotoxic agent may be a toxin (page 35, line 36). However, the specification neither disclose functional or structural attributes of a biological agent, nor any other therapeutic agent beyond than an antibody to PSM, which is conjugated to a toxin and binds to the surface of the prostate cancer cells. The specification does not teach particular structure of **the "biological agent"** except antibody, which could

bind to the PSM. The specification does not provide any method to ablate or kill cancerous prostate epithelial cells or a working example, which enables any biological agent conjugated to a toxin to bind to or kill the cancerous prostate epithelial cells. Therefore, one skilled in the art would not know how to use the claimed biological agent other than an antibody based on the teachings in the prior art or instant specification.

Biological agent reads on the agents being a DNA, organic molecule, protein, small peptide, carbohydrate etc. This reads on a multitude of compounds that are structurally unrelated. Applicants have not provided any guidance as to what part of the outer membrane domain needs to be targeted to result in the killing of the cancer cells, nor have the applicants determined minimal structure required by the agent to affect its activity. In the absence of this minimal structure, applicant would have to screen million of compounds to determine which has the ability to kill cancer cells.

In view of the lack of guidance, lack of examples, and lack of predictability associated with regard to the activity of claimed method of abating or killing cancerous prostate cells comprising binding of the biological agent to the outer membrane domain of the PSM antigen, one skilled in the art would be forced into under experimentation in order to practice the broadly claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 21-22, 25 and 27-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Brinkmann et al., (PNAS, vol 90, page 547-551, March, 1993).

The set of claims are drawn to a method of killing normal, benign or cancerous prostate epithelial cells comprising binding toxin-conjugated antibody to the surface of the cells.

Brinkmann et al., disclose a method of killing a prostate cancer cell with prostate antigen specific antibody conjugated with a toxin. Brinkmann et al., disclose that prostate carcinoma specific reacting antibody mAbPR1(Fv) is fused to a recombinant Pseudomonas exotoxin to, PR1(Fv)-PE38KDEL (page 548, column 2). Brinkmann et al., then disclose that the immunotoxin, PR1(Fv)-PE38KDEL, specifically binds to adnocarcinoma of the prostate tissue and prostate carcinoma cells (page 548 and 549, fig 1 and 4). Brinkmann et al., also disclose that the immunotoxin, PR1(Fv)-PE38KDEL, is specifically cytotoxic to the prostate cancer cells (page 550, table 1 and fig 5).

2. Claims 21-25 and 27-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Chu et al., (US Patent, 4939240, July 1990) or Horoszewicz et al., (US Patent, 5162504, Nov, 1992).

Claims 21-22, 25, 27-30 are set forth above. Claims 23-24 and 31 further drawn to claims 21, wherein the biological agent comprising a pharmaceutically acceptable carrier is administered to a mammal and bound to the PSM and kill the cells.

Chu et al., disclose a method of treating a cancer comprising a prostate carcinoma by monoclonal antibodies in conjunction with a pharmaceutical or cytotoxic agent, such as diphtheria toxin or ricin toxin (column 7, line 22-30, and column 14, section 5.8.3 and table VIII). Chu et al., also disclose an example of treating a breast cancer with the antibody or antibody conjugate being administered to mice bearing a tumor, which results in a rapid reduction of tumor size (column 44, line 15-28). Chu et al., further disclose that extensive necrosis of tumor cells were demonstrated in the tissue from the mice injected with antibody or antibody-toxin conjugate (column 44, line 63-70).

Horoszewicz et al., disclose a method of treating prostate cancer with prostate antigen specific antibody conjugated with a toxin (column 7, line 25-30). Horoszewicz et al., also disclose that the antibody with a pharmaceutical carrier is used to treat human prostate carcinoma patient in conjunction with a toxin either non-covalent or covalent linkages (column 11-12). Horoszewicz et al., further disclose that conjugated antibodies can be administered to patients to achieve enhance tumoricidal effects through the cytotoxic action (column 13, line 7-13).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-4.30pm Monday to Friday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lei Yao, Ph.D.
Examiner
Art Unit 1642

LY

Sheela J. Huff
SHEELA HUFF
PRIMARY EXAMINER